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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,877	06/28/1999	VIRGINIA M.-Y. LEE	PENN-0583	1398

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EXAMINER

BUNNER, BRIDGET E

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 02/08/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

09/297,877

LEE ET AL.

Examiner

Art Unit

Bridget E. Bunner

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 November 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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**DETAILED ACTION*****Status of Application, Amendments and/or Claims***

The amendment of 16 November 2001 (Paper No. 13) has been entered in full. Claims 1 and 3 are cancelled and claim 2 is amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 2 is under consideration in the instant application.

***Withdrawn Objections and/or Rejections***

1. The objections to the specification at pg 3-4 of the previous Office Action (Paper No. 11, 22 May 2001) are *withdrawn in part* in view of the amended trademarks and first line of the specification (Paper No. 13, 16 November 2001). Please see section on Specification below.
2. The objections to claim 2 at pg 4 of the previous Office Action (Paper No. 11, 22 May 2001) are *withdrawn* in view of the amended claim (Paper No. 13, 16 November 2001).
3. The rejection of claim 2 under 35 U.S.C. § 112, second paragraph at pg 6-7 of the previous Office Action (Paper No. 11, 22 May 2001) are *withdrawn* in view of the amended claim (Paper No. 13, 16 November 2001).

***Specification***

4. The disclosure is objected to because of the following informalities:
  - 4a. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The basis for this rejection is set forth at pg 3 of the previous Office Action (Paper No. 11, 22 May 2001).

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Applicant's arguments (Paper No. 13, 16 November 2001), as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant indicates that a copy of the abstract which was published on the cover page of the PCT application of which this is the U.S. National Stage application is enclosed in the Reply. Applicant's arguments have been fully considered but are not found to be persuasive because there is no copy of the abstract on a separate sheet enclosed in the Reply.

***Claim Rejections - 35 USC § 112, first paragraph***

5. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pg 4-6 of the previous Office Action (Paper No. 11, 22 May 2001).

Claim 2 is directed to a method of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an increased processing of amyloid precursor protein in neuronal cells isolated from said patient wherein the increased processing of amyloid precursor protein into amyloid  $\beta$  peptides is detected as an increase in the level of amyloid- $\beta_{42}$  in said neuronal cells, and said increase in amyloid processing is indicative of the pathogenesis of Alzheimer's disease.

Applicant's arguments (Paper No. 13, 16 November 2001), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

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Applicant asserts that claim 2 has been amended to recite that the present invention is a method of diagnosing Alzheimer's disease in a patient which comprises detecting increased processing of amyloid precursor protein in neuronal cells isolated from a patient wherein the increased processing of amyloid precursor protein into amyloid  $\beta$  peptides is detected as an increase in the level of amyloid- $\beta_{42}$  in the neuronal cells. Applicant argues that the claim as amended is enabled by the teachings of the specification as filed.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification does not disclose any methods or working examples of diagnosing Alzheimer's disease in a patient comprising detecting in the patient's isolated neuronal cells an increase in the level of amyloid  $\beta_{42}$ . The specification and the claims do not provide any guidance as to the specific assay utilized to detect amyloid  $\beta_{42}$  in neuronal cells. Roher et al. (Proc Natl Acad Sci 90 : 10836-10840, 1993) disclose that in vascular tissue of Alzheimer disease brains, amyloid  $\beta_{42}$  is more prevalent than amyloid  $\beta_{40}$  (pg 10836, abstract). However, Roher et al. indicate that previous groups obtained the opposite result, most likely due to purification procedures that selectively removed the less soluble amyloid  $\beta_{42}$  peptide (pg 10836, ¶ 2). Therefore, in regards to the instant specification, the disclosure of a specific assay utilized to measure amyloid  $\beta_{42}$  in neuronal cells would be crucial for the claimed method. Furthermore, the specification of the instant application does not indicate the region in the patient's brain that the neuronal cells are isolated from. The specification also does not teach how the cells are isolated from the patient in such a way so that the patient remains alive after the procedure has been completed. Additionally, as discussed in the previous Office Action (Paper No. 11, 22 May 2001), the state of the art is such that the search for highly specific and sensitive biochemical markers of

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Alzheimer's disease has been disappointing (Diaz-Arrastia, R. Arch Neurol 58: 354-355, 2001; pg 354, pp 3). Studies of cerebrospinal fluid or blood levels of markers such as amyloid  $\beta_{40}$  and amyloid  $\beta_{42}$  show significant differences between Alzheimer's disease and control subjects, but with a significant overlap between the 2 groups and a rather modest magnitude of differences (pf 354, col 1-2; Table).

Due to the large quantity of experimentation necessary to isolate a patient's neuronal cells and to measure amyloid  $\beta_{42}$  in a patient's neuronal cells, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art (see Roher et al.), and the unpredictability of diagnosing Alzheimer's disease with amyloid  $\beta_{42}$  (see discussion and Diaz-Arrastia), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

3. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 2 is directed to a method of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an increased processing of amyloid precursor protein in neuronal cells isolated from said patient wherein the increased processing of amyloid precursor protein into amyloid  $\beta$  peptides is detected as an increase in the level of amyloid- $\beta_{42}$  in said

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neuronal cells, and said increase in amyloid processing is indicative of the pathogenesis of Alzheimer's disease.

The specification as originally filed does not provide adequate written description a method of diagnosing Alzheimer's disease in a patient comprising detecting in the patient an increased processing of amyloid precursor protein in neuronal cells isolated from said patient wherein the increased processing of amyloid precursor protein into amyloid  $\beta$  peptides is detected as an increase in the level of amyloid- $\beta_{42}$  in said neuronal cells, and said increase in amyloid processing is indicative of the pathogenesis of Alzheimer's disease. The claimed method is not expressly or clearly asserted, nor does it flow naturally from the specification.

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*Conclusion*

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB  
Art Unit 1647  
January 28, 2002

*Elizabeth C. Kummer*

ELIZABETH KUMMERER  
PRIMARY EXAMINER